

REMARKS

The claims pending in the Application after entry of the present Amendment will be claims 1-42 and 45-47. Claims 43-44 and claims 48-62 have been canceled without prejudice. Claim 41 has been amended to insert “-OAc” and “oxo” such that the dependency of claim 42 on claim 41 is correct. Claims 11, 12-15 and claims 23-25 have been amended to correct typographical and syntax errors. Claims 1 and 11 have been amended to delete hydrogen. No new matter has been added by these amendments. Applicant reserves the right to pursue any canceled subject matter in future applications that claim priority to the present application.

I. Improper Final Rejection

Applicant hereby requests that the finality of the Office Action mailed February 13, 2009, in the above-referenced case be withdrawn. As described below, the finality of the Office Action is premature.

A first Office Action was mailed November 26, 2007, that included a prior art rejection over WO01/046451 (Takeuchi et al.). Applicant responded to this rejection on February 26, 2008, and it was withdrawn in the second Office Action mailed June 6, 2008. The rejections in this second Office Action were based on a newly cited reference Journal of Antibiotics (2002), 55(4), 442-444, Nakamura et al, and Tetrahedron Letters (2002), 43(5), 9039-9042, Gaul et al. The second Office Action also raised two separate 35 U.S.C. §112, 1st paragraph rejections and a 35 U.S.C. 2nd paragraph rejection. Applicant responded to these rejections on December 5, 2008, and all rejections were withdrawn in the third Office Action mailed February 13, 2009, except for one of the two previous 35 U.S.C. §112, first paragraph rejections, and the 35 U.S.C. §112, second paragraph rejection. The third, “Final”, Office Action also raised a new 35 U.S.C. §102(b) rejection that is based on a newly cited reference, GB 1036084.

MPEP §706.07(a) recites the following: “second or any subsequent actions on the merits shall be final, *except where the examiner introduces a new ground of rejection that is [not] necessitated by applicant’s amendment of the claims*” (emphasis added). Applicant respectfully submits that the new ground of rejection in this third Office Action was *not* necessitated by any of the claim amendments that Applicant made in the response filed December 5, 2008. The amendments made in the December 5, 2008, response substantially *narrowed* the claim scope. Nonetheless, the Examiner levies a *new* 102(b) rejection, based on GB 1036084. If GB 1036084

anticipated the amended claims, then it must also have anticipated the previously pending, broader claims. Thus, the examiner could have relied upon GB 1036084 in the second Office Action.

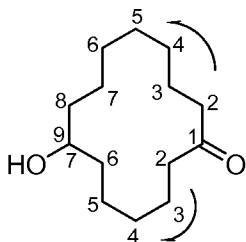
As noted in MPEP §706.07, “before final rejection is in order a clear issue should be developed between the examiner and applicant” and “switching [...] from one set of references to another by the examiner in rejecting in successive actions *claims of substantially the same subject-matter*, will [...] tend to defeat attaining the goal of reaching a clearly defined issue for an early termination” [emphasis added by Applicant].

Applicant respectfully submits that no clear issue has arisen in this case because the Examiner has simply switched from one set of references to another in order to reject claims of substantially the same subject-matter. In light of these facts, Applicant respectfully requests that the finality of the third Office Action be removed.

Notwithstanding the above, the Examiner has levied an improper §102(b) rejection over GB 1036084 as explained below.

II. **Rejection under 35 U.S.C. §102(b)**

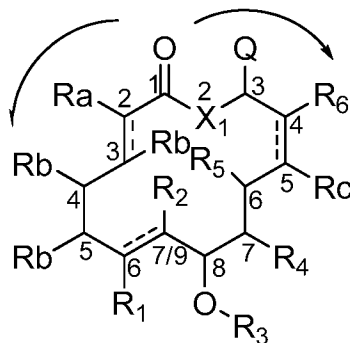
Claims 1, 11, 16 and 27 are rejected under 35 U.S.C. §102(b) as being anticipated by GB 1036084. According to the Examiner, GB 1036084 anticipates claims 1, 11, 16 and 27 because it teaches 7-hydroxycyclotetradecanone of the below structure:



7-hydroxycyclotetradecanone

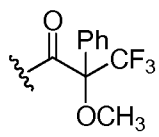
Respectfully, the Examiner is incorrect, as the compounds of Formula I recited in the present claims do not encompass 7-hydroxycyclotetradecanone. Specifically, 7-hydroxycyclotetradecanone is a 14-membered ring system wherein a hydroxy substituent is present at the 7th carbon of the system (i.e., the carbonyl moiety is the 1st carbon of the ring system). Alternatively, counting counter-clockwise around the ring, the hydroxy substituent is present at the 9th carbon of the ring system.

By contrast, Applicants' present claims recite Formula I, as depicted below (in the embodiment where $n=3$).



Applicants' Formula I wherein $n=3$

Specifically, substituent " R^2 " is at the 7th/9th carbon of Applicants' ring system. " R^2 " does not allow for hydroxy substitution in Applicants' claims. Hydroxy substitution at the 7th/9th carbon position would be required in order for GB 1036084 to anticipate the claimed genus. It is at least for this reason that GB 1036084 does not anticipate Applicants' claims. Additionally, Applicants' compounds require an " $-OR_3$ " substituent at the 8th carbon from the carbonyl moiety, whereas 7-hydroxycyclotetradecanone requires only hydrogen at that position. Applicant notes that R_4 = hydrogen has been deleted from the current claim scope thereby

requiring substitution of the 7th carbon by halogen, $-OR^{4A}$, oxo, $-OC(=O)R^{4A}$,  or $-NR^{4A}R^{4B}$, providing yet more differences from the cited compound. Therefore, Applicant respectfully submits that GB 1036084 cannot anticipate (or render obvious) the presently claimed invention.

Accordingly, Applicant submits that the rejection under 35 U.S.C. §102(b) should be withdrawn.

II. Rejection under 35 U.S.C. §112, para. 1

The Office Action maintains a rejection of claims 48-62 are rejected under 35 U.S.C. §112, first paragraph, on the ground that "the specification does not reasonably provide enablement for treating breast tumor metastasis in a subject." (see page 3 of the Office Action). Specifically, the Examiner has indicated:

“Applicant has narrowed the scope of the claims, however, the data potentially supporting a method for treating a breast tumor was still far more narrow than the scope of the claims. This conclusion was based on the few data points provided on a very limited number of compounds in the specification. If Applicant has a data compilation supporting the enablement of the claimed scope, the examiner would be willing to withdraw the rejection.”

Applicant respectfully disagrees with the Examiner. Not only did Applicant present amendments in their previous response that narrowed the claimed genus of compounds substantially, but the specification sufficiently enables compounds treatment of breast cancer. In fact, Applicant presented data directed to inhibition of lung metastasis in Example 57 (paragraph [0559]), which corresponds to Figure 4. Thus, the data set forth by Applicant regarding lung metastasis is sufficiently predictive of inhibition of breast metastasis, as presented in Example 56 (paragraph [0556]. Applicant additionally articulates at paragraph [0241] the following relationship between lung metastasis and breast metastasis:

“The highly aggressive and invasive 4T1 cells are routinely used as model for evaluating test compounds for the treatment of human ***breast cancer***, because the progressive spread of 4T1 cells to lymph nodes, ***lungs*** and other organs can be seen to ***mimic metastasis of human mammary cancer***.”
[Emphasis added by Applicant].

Moreover, Applicant also demonstrates that particular compounds do in fact work to treat breast cancer, see Examples 56-57 and Figure 4.

Notwithstanding the above, in order to expedite prosecution, Applicants cancels claims 48-62 such that the rejection under 35 U.S.C. §112, paragraph 1 is rendered moot.

V. **Rejection under 35 U.S.C. §112, para. 2**

Claims 43-44 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner asserts that:

“...there is not a sufficient disclosure to support enablement of the method of treating breast cancer as it would require undue experimentation, similarly, one of ordinary skill in the art would need to practice undue experimentation to arrive at the appropriate dosage level.”

Applicant respectfully disagrees with the Examiner. Applicant maintains that the teachings of the present specification as outlined by Applicant (at page 30) of the December 5, 2008, response provide clear guidance regarding the meaning of the phrase “an amount effective to inhibit metastasis/angiogenesis.” Furthermore, Applicant submits that one skilled in the art would clearly know how to optimize a dose(s), particularly when provided with: (a) the multiple biological assays as provided throughout the instant specification; (b) data showing that particular compounds act to treat breast cancer (see Examples 56-57 and Figure 4); and (c) the dosage level limitations in claims 1-10.

Moreover, the Examiner has set forth no argument, factors, reasons or evidence as to why one skilled in the art would need to perform “undue experimentation” as required by MPEP §2164.04.

Notwithstanding the above, in order to expedite prosecution, Applicants cancels claims 43-44 such that the rejection under 35 U.S.C. §112, paragraph 2 is rendered moot.

In light of the above Remarks and Amendments, Applicant respectfully submits that the present case is in condition for allowance. A Notice to that effect is respectfully requested. Applicants invite the Examiner to contact the undersigned, Julie Anne Knight, at (617) 248-5227, with any questions pertaining to the above-identified application in order to expedite prosecution of this case.

Respectfully submitted,

Dated: April 7, 2009

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